Kidney International, Vol. 14 (1978), pp. 486–490

Influence of exchange volume and dialysate flow rate on solute clearance in peritoneal dialysis

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Influence of exchange volume and dialysate flow rate on solute clearance in peritoneal dialysis. To find the ideal dialysate flow rate and exchange volume for use in long-term peritoneal dialysis, 10 patients were studied over a period of 1.5 yr. Exchange volumes of 1 or 2 liters and dialysate flow rates of 1, 2, 3, 4, and 6 liters/hr were tested. Dextrose concentration remained constant at 1.5 g/100 ml. Peritoneal clearances for BUN, creatinine, and uric acid were calculated at 2, 5, 10, 15, and 20 hr during dialysis making a total of 120 clearances for each patient. All patients used a reverse osmosis automatic machine. The clearances of all three solutes tended to be higher with exchange volumes of 2 liters than they did with 1 liter; this trend was significant for BUN ($P < 0.025$) and uric acid ($P < 0.025$) but not for creatinine. There was a significant rise in clearance with increasing flow rates per hour for all solutes as shown in the following table.

Flow rate *liters/hr*	Mean clearance, *ml/min/2-liter exch.*		
	Creatinine	BUN	Uric acid
2	13	22	10
3	14	22	10
4	19	26	14
6	23	30	17

Since patients could not tolerate a flow rate of 6 liters/hr, we conclude that a flow rate of 4 liters/hr with a 2-liter exchange will give maximum efficiency.

Influence du volume d'échange et du débit de dialysat sur les clairances des substances dissoutes dans la dialyse péritonéale. Afin de déterminer le débit idéal de dialysat et le meilleur volume d'échange dans la dialyse péritonéale prolongée, 10 malades ont été étudiés sur une période d'un an et demi. Des volumes d'échange de 1 ou 2 litres et des débits de dialysat de 1, 2, 3, 4 et 6 litres/heure ont été essayés. La concentration de dextrose a été constante à 1,5 g/100 ml, les clairances péritonéales de l'azote uréique, de la créatinine, de l'acide urique ont été calculées à 2, 5, 10, 15 et 20 heures au cours de la dialyse, soit au total 120 clairances pour chaque malade. Tous les malades ont utilisé un appareil automatique d'osmose inverse. Les clairances des trois substances tentent à être plus élevées avec un volume de 2 litres qu'avec un volume de 1 litre. Cette tendance est significative pour l'azote uréique ($P < 0,025$) et l'acide urique ($P < 0,025$) mais pas pour la créatinine. Il y a une augmentation significative des clairances quand le débit horaire augmente ainsi qu'il est indiqué dans le tableau ci-dessous.

Debit *litre/hr*	Clairance moyenne, *ml/min/cycles de 2 litres*		
	Créatinine	azote uréique	acid urique
2	13	22	10
3	14	22	10
4	19	26	14
6	23	30	17

Du fait que les malades ne peuvent pas supporter les débits de 6 litres/hr, nous concluons qu'un débit de 4 litres/hr avec un volume de 2 litres doit donner le maximum d'efficacité.

Received for publication March 15, 1978;
and in revised form April 28, 1978.

0085-2538/78/0014–0486 $01.00

During the past few years, there has been an increasing realization that peritoneal dialysis is a worthwhile alternative to hemodialysis in the treatment of end-stage renal failure [1, 2].

As the indications for peritoneal dialysis expand and more nephrologists have experience with this technique, it becomes important to define the optimum condition for maximal dialysis efficiency. The present study has analyzed the effects of different exchange volumes and dialysate flow rates on peritoneal clearance and solute removal on patients undergoing long-term peritoneal dialysis. In addition, we have established baseline data so that comparison can be made when the standard intermittent dialysis technique is compared with newer methods of dialysis.

Methods

Ten patients undergoing long-term peritoneal dialysis were studied; the period of study was 1.5 yr. There were six men and four women; all had a permanent peritoneal dialysis catheter. The duration of dialysis prior to the study varied from 4 to 36 months of peritoneal dialysis, with an average of 12 months. During the study, all patients were dialyzed in a center unit with a reverse osmosis peritoneal machine. Each patient received 20 hr of dialysis, twice weekly. The dialysate dextrose was kept constant at 1.5 g/100 ml throughout the study. We used exchange volumes of 1 and 2 liters, and for each exchange volume varied the dialysis flow between 2, 3, 4, and 6 liters/hr. A typical cycle using an exchange volume of 1 liter consisted of an inflow time of 5 min and an outflow time of 5 min. Since we only chose patients who had good catheter function, a rapid inflow and outflow was obtained in all patients, and only the dwell time was varied, so that for 2 liters/hr of flow, we had a dwell time of 20 min; for 3 liters, a dwell time of 10 min; for 4 liters, a dwell time of 5 min; and for 6 liters, there was 0 dwell time. Similarly, for exchange volumes of 2 liters there was an inflow time of 10 min, and dwell times were 40, 20, 10, and 0 min, respectively. Clearance studies were done at 2, 5, 10, 15, and 20 hr of dialysis. Each clearance study lasted 1 hr, and blood samples were taken at the midpoint of the clearance study. Altogether, over the period of study, 2,000 clearances were performed in the 10 patients. The solutes studied were BUN, creatinine, phosphate, uric acid, and potassium. In addition, weight loss and protein loss during the dialysis were measured. Protein in the dialysate was measured by a modified Biuret test adapted for low protein concentration [3]. The protein concentration in each sample of dialysate over the 1-hr clearance period was calculated and assured to be unchanged until the next clearance period. The sum of the five periods was then calculated to give the total protein removed during a 20-hr dialysis. BUN was analyzed with a Technicon basic autoanalyzer; creatinine, phosphate, uric acid, and potassium were analyzed with a Technicon SMA-12/60 analyzer.

Statistical methods. The eight mean clearances of each solute were compared by the two-way classification of analysis of variance.

The mean clearance of each patient at 3, 5, 10, 15, and 20 hr of dialysis was broken down into factorial analysis in order to test: *1)* if the mean clearance of the 1-liter exchange volume is significantly different from that of 2 liters. *2)* If the mean clearances at flow rates of 2, 3, 4, and 6 liters/hr, when combined with 1- and 2-liter exchange volumes, are statistically different from each other.

Since the factorial analysis showed no interaction statistically, the mean clearances at the four different flow rates were tested for linearity and regression analysis. They all showed a linear trend with a positive slope.

Results

Fig. 1 shows the clearance of BUN, creatinine, and uric acid at different flow rates and exchange

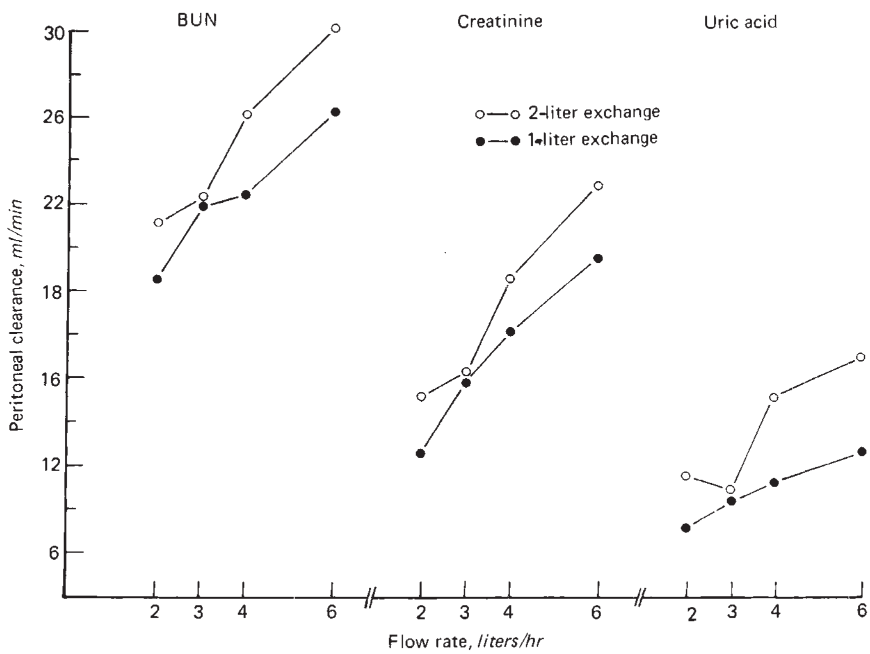

Fig. 1. *Relationship between flow rate of dialysate, exchange volume, and peritoneal clearance for BUN, creatinine, and uric acid.*

volumes. There was a linear increase of clearance with flow rates for all solutes studied. In addition, there was a trend for the 2-liter volume exchanges to have a higher clearance than the 1-liter volume exchanges, although this reached statistical significance only in BUN and uric acid. Abdominal girth and body weight were tested for correlation with clearance; there was, however, no statistical correlation between them.

Fig. 2 shows similar results with potassium and phosphate. Again, there was a linear increase of clearance with increasing flow rates of dialysis and a tendency for the 2-liter exchanges to be more efficient than the 1 liter was.

Fig. 3 shows the weight change during a 20-hr peritoneal dialysis with 1.5 g/100 ml glucose. This represents the mean of 10 patients for each particular dialysate flow rate. Increasing dialysate flow rates did not affect weight loss.

Fig. 4 shows the protein loss. There was no correlation between flow rates and protein loss. The mean protein loss with a 2-liter exchange was 9 ± 2.5 g/20 hr, and with a 1-liter exchange it was only 4 ± (SEM) 1.8 g, a highly significant difference ($P < 0.001$). There was, however, a large variation between individual patients.

Blood sugar concentrations during dialysis showed a small rise to a maximum of 132 mg/100 ml at 10 hr, which fell to 110 mg/100 ml after 20 hr of dialysis. Similar changes in blood sugar were seen with all other rates of dialysate flows studied.

Fig. 5 shows the plasma changes of different solutes during the 20-hr dialysis with a 4-liter/hr flow rate and 2-liter exchanges. As would be expected, there was a linear fall of all solutes studied. BUN fell by 30 mg/100 ml, creatinine fell by 2 mg/100 ml, uric acid fell by 1.7 mg/100 ml, and potassium fell by 0.8 mEq/liter.

Table 1 shows the mean ± 1 SEM of peritoneal clearance of all solutes studied at a flow rate of 4 liters/hr and an exchange volume of 2 liters.

Table 2 shows the average solute removed again at a 4-liter/hr flow and a 2-liter exchange volume ± 1 SEM.

Discussion

There are obviously a large number of factors which may influence peritoneal clearance. The first of these is the surface area of the peritoneum. The

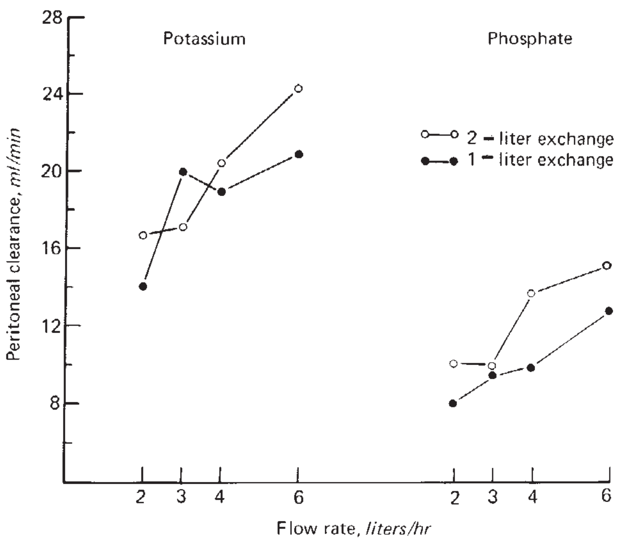

Fig. 2. *Relationship between flow rate of dialysate, exchange volume, and peritoneal clearance for potassium and phosphate.*

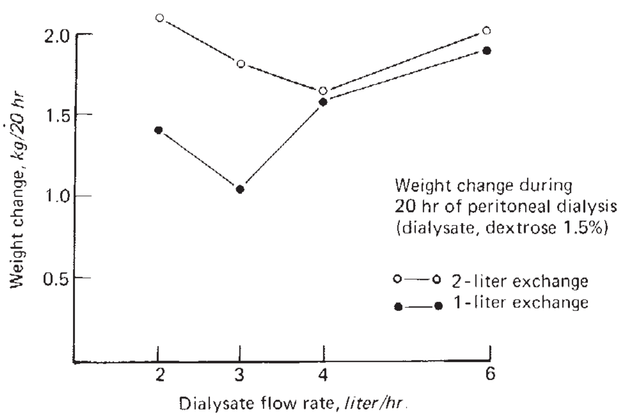

Fig. 3. *Relationship between dialysate flow rate, exchange volume, and weight loss.*

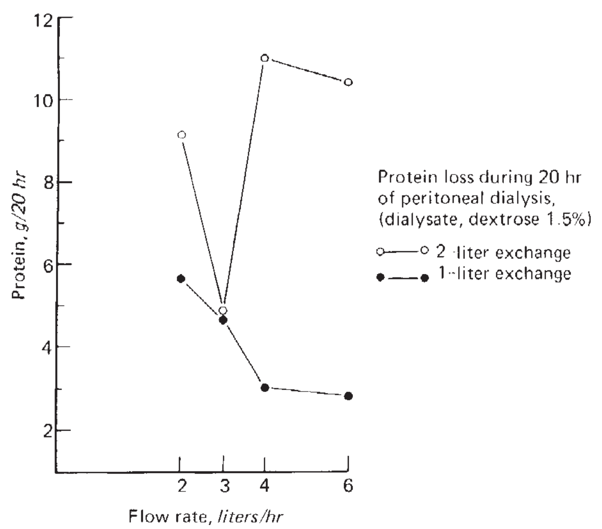

Fig. 4. *Relationship between dialysate flow rate, exchange volume, and protein loss.*

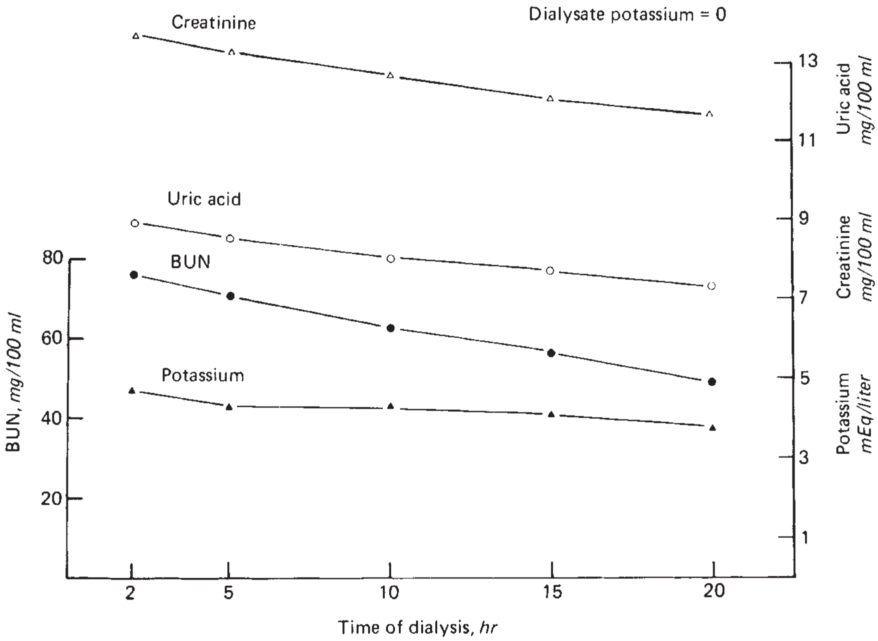

Fig. 5. *Showing linear fall in creatinine, uric acid, BUN, and potassium over a 20-hr dialysis period.*

Table 1. Mean ± SEM of peritoneal clearances (ml/min) at flow rate of 4 liters and exchange volume of 2 liters

Creatinine	18.6 ± 3.2
BUN	26.2 ± 2.4
Uric acid	13.2 ± 2.8
Phosphate	14.0 ± 2.7
Potassium	20.4 ± 2.2

Table 2. Mean ± SEM of solute removal at 20-hr peritoneal dialysis with flow rate of 4 liters/hr and exchange volume of 2 liters/hr

Creatinine, *mg*	1913 ± 290
BUN, *g*	18 ± 2.4
Uric acid, *mg*	1100 ± 218
Phosphate, *mg*	800 ± 130
Potassium, *mEq*	96 ± 8.7
Protein, *g*	11.4 ± 3.6

peritoneal surface area is about 1.0 m^2 for an average size person [4]. In over 2,000 clearances that we examined, there was no correlation between clearance, body weight, and abdominal girth, so that individual variation in size could not account for variation in clearance. It has been reported that peritoneal clearance decreases progressively with the months on dialysis [5]. We therefore compared the average clearance of the group with the length of time the patients were on dialysis, but we could not find a correlation. Clearance is also related to ultrafiltration, especially when using high concentrations of dextrose [6]. During clearance studies, the glucose was maintained constant at 1.5 g/100 ml for the duration of the dialysis. Since patients usually required higher concentration for fluid removal, the study was done only once weekly in patients; the second weekly dialysis with a higher concentration of dextrose was not included in the study. The main factor controlling the clearance of small solutes seems to be the dialysate flow rates. Boen [7] has stated that with increasing dialysate flow rates, the peritoneal clearance falls off. This, however, was shown by Tenckhoff, Ward, and Boen [8] and by Boen [9] to be due to statistical error; Tenckhoff showed that, in fact, the clearance can be increased with dialysate flows up to 12 liters/hr. Our results confirm this observation; since in our hands, however, flow rates of dialysates of 6 liters/hr caused the patients' abdominal pain. We have adopted a compromise and suggest that a flow rate of 4 liters/hr is best tolerated and gives maximum efficiency. The break in the curves seen at 3 hr with the 2-liter volume exchanges is probably due to an artefact. This was due to the technical difficulty of stopping a patient's drainage in the middle of the cycle to get an exact drainage volume of 3 liters. We therefore collected two 2-liter samples and took 75% of these as representing a drainage volume of the 3 liters.

The small drop in serum potassium concentration of 0.8 mEq/liter following 20 hr of dialysis reflects the relatively low efficiency of peritoneal dialysis on potassium removal. The average potassium clearance of 20 ml/min at a maximum diffusion gradient (dialysate potassium = 0) is in agreement with Brown, Ahearn, and Nolph [10]. Although none of our patients were hyperkalemic, it has been calculated by Brown et al [10] that the maximal removal of potassium in peritoneal dialysis in a hyperkalemic patient is 12.5 mEq/hr, using hypertonic glucose which accentuates potassium removal. The efficacy of peritoneal dialysis in lowering potassium concentration during acute hyperkalemia is, therefore, probably related to changes in blood bicarbonate concentration and the rapidity with which dialysis can be started.

With regard to dialysate volume, Goldschmidt et al [11] found that 1-liter exchange volumes were comparable in efficiency to 2-liter exchange volumes. Although our data suggests that 2-liter volumes are slightly more efficient than 1-liter exchange volumes, we would agree that where congestive cardiac failure is present or patients cannot tolerate such high volumes, then 1-liter volume exchanges would be equally satisfactory.

The 2-liter exchange volumes removed twice as much protein as did the 1-liter exchange volumes. Since the dwell times with the 2-liter exchanges were double that of the 1-liter exchanges, it is possible that the peritoneal surface was irritated by the more prolonged contact and that this resulted in an increased protein loss with the 2-liter exchanges. This is in agreement with the work by Strauch et al [12] who found that a longer time cycle was associated with increased protein loss.

Phosphate clearances were low, and the total amount of phosphate removed was 806 mg/20 hr of dialysis during ideal flow conditions. This would explain the tendency for patients to have a high serum phosphate concentration and the frequency of progressive bone disease which has been found [13].

The creatinine clearances were within the range generally reported for peritoneal dialysis; the fall of serum creatinine, however, was only 2 mg/100 ml per 20 hr of dialysis, reflecting the relatively low peritoneal clearance for creatinine with this method. Since neuropathy often progresses in patients on peritoneal dialysis [13] and since in our experience it only does so in the presence of a high serum creatinine concentration, we believe that every effort should be made to decrease the creatinine by increasing dialysate flow rates to 4 liters/hr.

At present, the high costs of commercially available solutions limit the cost effectiveness of increasing dialysate flows for all patients. Nevertheless, for the occasional patient who shows signs of underdialysis, increasing dialysate flow rate may be a good method of treatment.

The extensive baseline data which we have established will serve as a model when comparing newer methods of dialysis.

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